APPENDIX I: Declaration of Janet D. Rowley, M.D., D.Sc., including Exhibit 1, *Curriculum Vitae* of Janet D. Rowley.

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Olufunmilayo I. Olopade

Serial No.: 08/674,311

Filed: July 1, 1996

For: METHYLTHIOADENOSINE PHOSPHORYLASE COMPOSITIONS AND METHODS OF USE IN THE DIAGNOSIS AND TREATMENT OF PROLIFERATIVE DISORDERS

Group Art Unit: 1655

Examiner: L. Arthur

Atty. Dkt. No.: ARSB:509—1

CERTIFICATE OF MAILING
37 C.F.R. § 1.8

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as First Class Mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231, on the date below:

7 June 2002 Thomas M. Boyce
Date Thomas M. Boyce

DECLARATION OF JANET D.ROWLEY, M.D., D.Sc.

I, Janet D. Rowley, hereby declare as follows:

1. I am The Blum-Riese Distinguished Service Professor in the Departments of Molecular Genetics & Cell Biology, of Medicine and of Human Genetics, University of Chicago, 5841 South Maryland Ave., MC 2115, Chicago, Illinois 60637. I have extensive experience in the study of molecular genetics and in the techniques and knowledge required of gene cloning, mapping, and molecular biology. References containing examples of my work are included in my *Curriculum Vitae*. A copy of my *Curriculum Vitae* is attached as Exhibit 1.

2. I understand that the patent examiner in charge of assessing the patentability of the above-referenced application has rejected the claims of that application. I have reviewed the

Final Office Action dated March 15, 2001, the pending claims, and the reference asserted by the examiner in rejecting the claims: Kamb, AK, NA Gruis, J Weaver-Feldhaus, Q Liu, K Harshman, SV Tavtigian, E Stockert, RS Day, BE Johnson, and MH Skolnick (1994) *Science* 264:436-440. I am providing this declaration to submit additional information relating to this application.

3. The present application refers to gene sequences encoding methylthioadenosine phosphorylase (MTAP). I understand that the Examiner believes that Kamb et al. (1994) describes clones of human sequences that contain at least part of the gene encoding MTAP. However as noted below (4) the examiner is not correct in stating that the "large isolated polynucleotide which contains somewhere within its structure the nucleic acid sequence encoding the MTAP polypeptide." The cosmid used was 849 base pairs (0.849 kb) in length. MTAP is about 80,000 base pairs distal from this clone.

4. Upon reading and studying the text, figures, and references of Kamb et al. (1994) I can find no evidence that any of the clones found in Kamb et al. (1994) necessarily contain or are likely to contain any part of the gene encoding MTAP. In fact research published from my laboratory (S Gursky, OI Olopade, and JD Rowley (2001) *Cancer Genetics and Cytogenetics* 129: 93-101) clearly shows (see Figure 2) that MTAP is about 80kb distal to MST1 (CDKN2A). Therefore <u>none</u> of the clones in Kamb et al, Figure 1 are within about 50kb of MTAP.

5. The clones described in Kamb et al. (1994) are a series of cosmids and P1 phage clones that span a region of a total of about 50 to 40 kb, including no more than 10 to 20kb to either side of the MTS1 and MTS2 loci. However, in order to determine whether these clones contain any other genes of interest they would either have to be completely sequenced or other,

independent data would have to exist that would allow the inference that the MTAP gene was contained in the cloned region.

6. Kamb et al. (1994) do not present any sequence data other than those of the MTS1 and MTS2 loci (see Figure 2). Their sequence data thus do not indicate that a gene encoding MTAP exists in their clones.

7. Kamb et al. (1994) also do not provide any other data suggesting that the cloned region contains a gene for MTAP. Such data could include the presence of genetic markers further distal or proximal to MTS1 and MTS2 that are known to bound the region containing the MTAP gene. However, Kamb et al. (1994) do not show or discuss such markers. The markers used are not known to bound the region containing the MTAP gene. No other data are provided that might suggest that the gene for MTAP lies in the cloned region. In fact, Kamb et al. (1994) never discuss whether the MTAP gene lies in the region at all.

9. Based upon my skill and training in the area of molecular biology and genetics, I can say that there is no evidence whatsoever in the Kamb et al. (1994) paper that would lead one to conclude that the gene for MTAP is contained in any of the clones Kamb et al. made.

10. I declare that all statements made of my knowledge are true and all statements made on the information are believed to be true; and, further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under § 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this application or any patent issued thereupon.

Date: June 6, 2002

Janet D. Rowley

Janet D. Rowley, M.D.